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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,867	06/15/2001	Pierre Carol	109326	6258

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EXAMINER
KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/807,867	Applicant(s) CAROL ET AL.	
	Examiner Russell Kallis	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *2, 4-6, 8, 11, 15-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7,9,10 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 15 is acknowledged. The traversal is on the ground(s) that Groups I-IV have unity of invention. This is not found persuasive because the claims are not linked by a corresponding special technical feature because they do not constitute an advance over the prior art. This is made clear in the office action under the 35 U.S.C. 102(b) rejections showing that the isolated polynucleotide of SEQ ID NO: 1 encoding a polypeptide of SEQ ID NO: 2 of either Carol P. *et al.* or Wu D. *et al.* anticipates the inventions of Claims 1 and 3.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 7, 9, 10, and 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1: improper Markush terminology. Insert --or-- after the comma at the end of the first paragraph of the claim. See MPEP 2173.05(h).

Claim 10: "origin of replication of the transcription of the plants" is contrary to art recognized terminology. See MPEP 2173.03 and 2173.05(a).

Claims 1, 3, 9, and 13: recitations of "particularly" or "more particularly" fail to positively recite required claim elements. It is unclear whether the subject matter recited after "particularly" is merely exemplary or in fact required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 7, 9, 10, and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims an isolated polynucleotide of SEQ ID NO: 1 encoding a TOCB of SEQ ID NO: 2 and modified polynucleotides encoding modified polypeptides or a fragment thereof having TOCB activity equivalent to the enzyme in the plant.

Applicant describes an isolated polynucleotide of SEQ ID NO: 1 encoding a polypeptide of SEQ ID NO: 2 having TOCB activity equivalent to the enzyme in the plant.

Applicant does not describe any modified variants of SEQ ID NO: 1 encoding any modified polypeptides or fragments thereof having TOCB activity equivalent to the enzyme in the plant.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism

and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Given the failure of the TOCB DNA to be adequately described, methods of its use are also inadequately described. See Written Description Guidelines, Federal Register Vol. 66 No. 4, Friday January 5, 2001 "Notices", pages 1099-111.

Claims 1, 3, 7, 9, 10, and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant broadly claims an isolated polynucleotide of SEQ ID NO: 1 encoding a TOCB of SEQ ID NO: 2 and modified polynucleotides encoding modified polypeptides or a fragment thereof having TOCB activity equivalent to the enzyme in the plant and a method for producing and increasing carotenoid biosynthesis in a plant transformed with said isolated DNA.

Applicant teaches isolation of a cDNA encoding a TOCB from an *Arabidopsis* cDNA library using a TOCB genomic fragment isolated from an Ac/Ds mutagenized *Arabidopsis* population (Example 1 pages 14-18), isolation of cDNA from tomato and *Capsicum*

corresponding to the TOCB isolated from *Arabidopsis* (Example 4 page 21), expression of the *Arabidopsis* TOCB cDNA in *E. coli*, and measurement of cyanide resistant oxygen consumption characteristic of TOCB enzymes (Example 6 pages 23-26).

Applicant does not teach TOCB activity encoded by any other cDNA sequences other than SEQ ID NO: 1 and plants transformed with said cDNA having production of or increased production of carotenoids.

Isolation of closely related polynucleotide sequences having the same or equivalent activity is unpredictable. The lack of guidance as to which point mutations would best serve the invention or which fragments of TOCB enzyme best retain activity in a plant would require one of skill in the art to test *in planta* for induction of gene expression or carotenoid biosynthesis. Cloning the large number of constructs and making the transgenic plants comprising those constructs to find a polynucleotide encoding a full length or a fragment of a TOCB enzyme having activity in plants would require undue experimentation to make and use the invention.

The limitation introduced in isolating an equivalent sequence encoding the same protein activity is illustrated in an example where a small number of changes to the coding region for a strict desaturase resulted in an enzyme with a hydroxylase activity and that a small number of changes to the coding region of a desaturase could account for the functional divergence seen across a range of enzymes involved in fatty acid metabolism (Broun P. *et al.* Science Vol. 282; 13 November 1998, pp. 1315-1317; Abstract lines 4-6 and p. 1317 column 1, lines 37-56).

The *immutans* phenotype has been shown to be a mild or leaky phenotype because it can develop green sectors under moderate light, suggesting that there are alternative mechanisms for carotenoid biosynthesis and that the role of TOCB in carotenoid biosynthesis is as a co-factor for

phytoene desaturation, and indicating that phytoene desaturase levels would ultimately limit any attempt to increase carotenoid levels by over expression of TOCB (Carol P., *et al.* Trends in Plant Science; Jan. 2001; Vol. 6, No. 1; pp. 31-36; from page 33 column 2 to page 34 column 1).

Moreover, constitutive expression of a phytoene synthase redirected metabolites from the giberellin pathway and stunted plant growth creating a dwarf phenotype, underscoring the intricate regulation of the carotenoid/phytoene biosynthetic pathway and that engineering of this pathway indiscriminately in all plant tissues is fraught with unpredictability (Fray R. *et al.* The Plant Journal 1995; Vol. 8, No. 5; pp. 693-701; Abstract and p. 700 column 1, lines 1-19).

Given the lack of guidance for isolating any other equivalent TOCB gene or fragment thereof, or for producing plants transformed with TOCB genes or any other non-exemplified gene equivalents of SEQ ID NO: 1, given the breadth of the claims and the unpredictability in the art, undue trail and error experimentation would be needed by one skilled in the art to isolate a multitude of non-exemplified TOCB genes, or to evaluate the ability of a multitude of non-exemplified TOCB genes or non-exemplified gene fragments to alter the phenotype of a multitude of transformed plant species. Therefore, the invention is not enabled.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The DNA of claims 1 and 3, since it has not been isolated by the hand of man reads as a product of nature, thus falling outside the five classes of patentable subject matter. The DNA molecule, as claimed, has the same characteristics and

utility as those found naturally in the genome or as cellular precursors thereof and therefore does not constitute patentable subject matter. See *American Wood v. Fiber Distintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Carol P., *et al.* (GenBank Accession Number AJ004881, submitted March 8, 1998).

Carol teaches an isolated polynucleotide of SEQ ID NO: 1 inserted into a vector comprising heterologous sequences and encoding a TOCB polypeptide of SEQ ID NO: 2; thus the reference teaches all the limitations of Claims 1 and 3 and 7.

Claims 1, 3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu D., *et al.* (GenBank Accession Number AF098072, submitted October 9, 1998).

Wu teaches a cDNA having 99.9% sequence identity to SEQ ID NO: 1 inserted into a vector comprising heterologous sequences with a nucleotide substitution at position #1123 (T to A) encoding a TOCB protein having 99.8% sequence identity to SEQ ID NO: 2 (Accession number AF098072, submitted October 9, 1999); thus the reference teaches all the limitations of Claims 1 and 3. and 7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 7, 9, 10 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauptmann R. *et al.* U.S. Patent 5,618,988 in view of Carol P., *et al.* (GenBank Accession Number AJ004881, submitted March 8, 1998) or Wu D., *et al.* (GenBank Accession Number AF098072, submitted October 9, 1998).

Applicant claims an isolated polynucleotide of SEQ ID NO: 1 encoding a TOCB of SEQ ID NO: 2 and modified polynucleotides encoding modified polypeptides or a fragment thereof having TOCB activity equivalent to the enzyme in the plant, and a method for producing and increasing carotenoid biosynthesis in a plant transformed with said isolated DNA.

Hauptmann teaches carrot and potato transformed with plasmids comprising a tissue specific promoter, a transit peptide, and a phytoene synthase gene showing an increase in carotenoids in root and tubers (columns 33, 36, and 37).

Hauptmann does not teach an isolated polynucleotide of SEQ ID NO 1 encoding a TOCB enzyme of SEQ ID NO: 2.

The teachings of Carol and Wu are discussed supra.

It would have been obvious at the time of Applicant's invention to modify the invention of Hauptmann to substitute a polynucleotide encoding a TOCB enzyme taught by Carol for the phytoene synthase. One of skill in the art would have been motivated by the knowledge common

in the art that carotenoid biosynthetic genes are valuable materials for genetic engineering of plants and given the success of Hauptmann in enhancing the expression of carotenoids in carrot and potato transformed with a carotenoid biosynthetic gene, one would have had a reasonable expectation of success of expressing genes other carotenoid biosynthetic genes in plants and producing or increasing carotenoids thereby.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the receptionist, whose telephone number is (703) 308-0196.

Russell Kallis Ph.D.
February 21, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638